Proton imaging issues

Van Nguyen

2.19.09

Outline

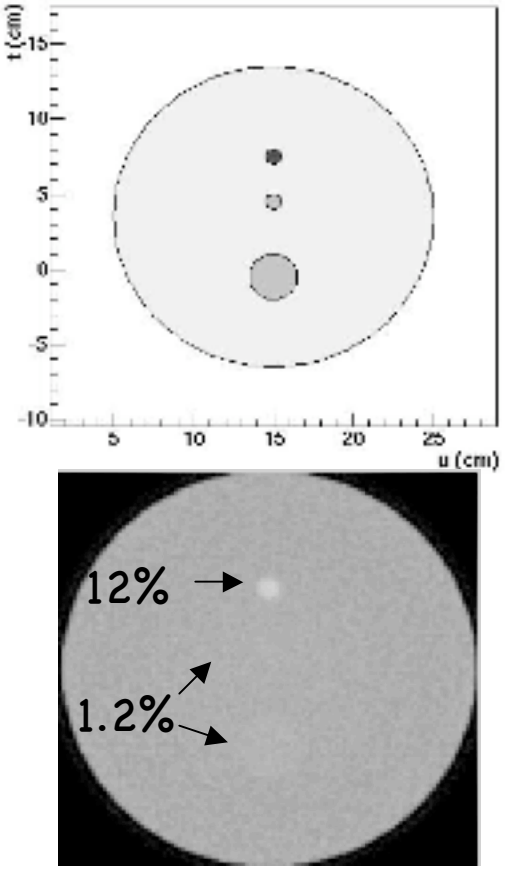
- Website updated
  - home.fnal.gov/~van619/muonsinc (usrnm: muonsinc, pwd: ptherapy)
- Information from R. Schulte, MD, Loma Linda University Medical Center
- Gold nanoparticles and pins
- The pCT Collaboration

R. Schulte Q&A

- Q: What is the range of tumor densities?
  - A: Density differences between different tumors and adjacent normal tissues are generally only a few percent or less.
- Q: Is tumor density different enough from normal tissue density to be detected via protons?
  - A: In principle, even small density differences can be made visible if one is willing to give a higher dose, which is problematic. A second possibility is to enhance tumors with contrast (see below).
- Q: Could we implant a dense material, say gold, into a tumor and track the gold as the tumor changes?
  - A: Yes that is a good idea in particular when one uses gold nanoparticles that track tumor cells. I proposed this idea a few years ago in a conference paper: Nanoparticle-enhanced proton computed tomography: a Monte Carlo simulation study. Schulte, R.; et al. D.C. Biomedical Imaging: Nano to Macro, 2004. IEEE International Symposium 2004 1354- 1356.

Gold nanoparticles

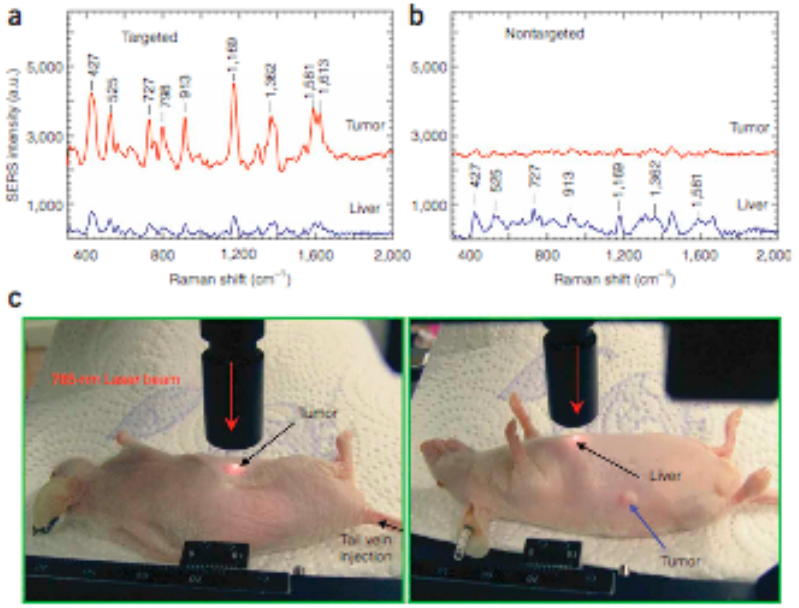
- Need to increase contrast of tumor tissues wrt to normal tissues
- Schulte et al. simulated 200 MeV protons going through a cylindrical water phantom with embedded inhomogeneities enhanced with traces of gold
- Method: bind 100 solid gold nanoparticles to the surface of tumor cells using cell-seeking antibodies conjugated to the surface of the nanoparticles
  - Antibody conjugation utilizes chemical linkages to produce affinity and binding of antibodies with another surface
  - For contrast of 1%, one needs to add 10 mg gold or 3E18 gold atoms
- Results: object with 12% density enhancement very well distinguished from background water signal; other two objects with 1.2% density enhancement are only faintly visible



Reconstructed image

Gold nanoparticles cont'd

- Shuming Nie, Ph. D. & Co. at Emory-Georgia Tech Nanotechnology Center for Personalized and Predictive Oncology, performed *in vivo* tagging of tumors with nanoparticles
  - See Nature Biotechnology Jan. 2008 (**26**) 1: 83:90.
- They used conjugation of nanoparticles with antibodies to target malignant tumors with high specificity and affinity. (To prepare a targeted nanoparticle, they used a version of polyethylene glycol (PEG) to which they could chemically link an antibody that binds to epidermal growth factor receptor (EGFR), a molecule overexpressed on many types of tumors.)

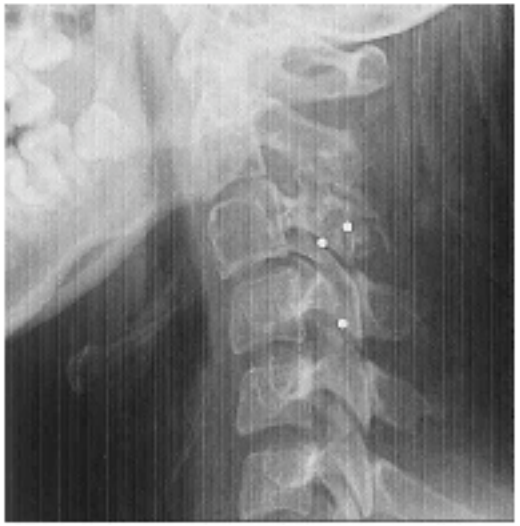


Raman scattering: inelastic scattering of photons

- They injected the targeted nanoparticles into mice with EGFR-positive human head and neck carcinomas and obtained **Surface Enhanced Raman Spectroscopy** (SERS) spectra 5 hours later (see figure). As control experiments, the researchers injected matching mice with untargeted nanoparticles. The unique optical spectra of the nanoparticles were easily detected in both sets of animals, but only the targeted nanoparticles accumulated in tumors. In contrast, the untargeted nanoparticles accumulated largely in the liver.

Gold pins

- Internal gold markers have been inserted into various organs for precise setup and real-time tumor tracking in radiotherapy (RT)
  - See, for example, Shirato, H. et al. International Journal of Radiation Oncology, Biology, Physics 2003;56(1):240-7.
    - Inserted 2.0 mmD gold markers into or near spinal, prostate, liver, and lung tumors.
    - Three markers were used to adjust the CM of the target volume to the planned position.
    - Marker implantation was successful and was used for real-time tumor tracking in RT in 90% of tumors
    - The distance between the three markers gradually decreased in some of the patients during RT



The pCT collaboration

- The pCT collaboration, headed by R. Schulte, is a collaboration between BNL, LLU, UCSC, and Stonybrook (http:/scipp.ucsc.edu/pCT/)
  - Objective: to apply the latest technology and computer algorithms to the use of low energy proton beams for medial diagnostic and therapeutic imaging
- pCT scanner conceptual design: the proton locations and directions at the entrance and exit of the phantom/patient are measured each with a telescope consisting of two x-y planes of silicon detectors with the energy of the exit proton measured by an array of calorimeter crystals (CsI)
- Have developed a data acquisition system capable of recording particle rates in excess of 1 MHz

See IEEE Trans. on Nuc. Sci. 2007 (**54**) 1: 140-145.

pCT collaboration cont'd

- Their simulation implements a theoretical Most Likely Path (MLP) prediction
- Have conducted beam experiments to track the MLP
  - 200 MeV proton beam tracked with silicon strip detectors (SSDs) and a CsI calorimeter cystal measured the energy
  - SSDs provided position resolution of ~80μm and angular resolution of ~3mrad
  - Agreement between data and MLP within 350 μm
- Next steps: beam test with an inhomogeneous absorber followed by CT studies using a rotating phantom

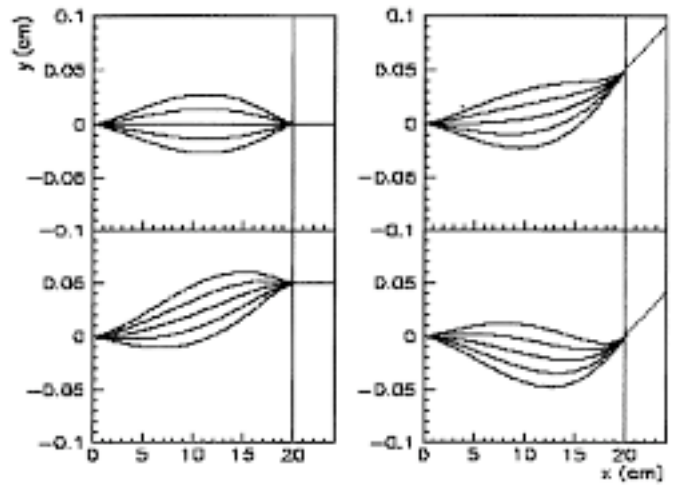


Fig. 1. Representative examples of MLPs including one- and 2-sigma envelopes of 200 MeV protons inside 20 cm of water [6]. These curves are colloquially called "bananas". Left side: zero exit angle, displacement 0 cm (top) and 0.05 cm (bottom). Right side exit angle 10 mrad, displacement 0.05 cm (top) and 0 (bottom).

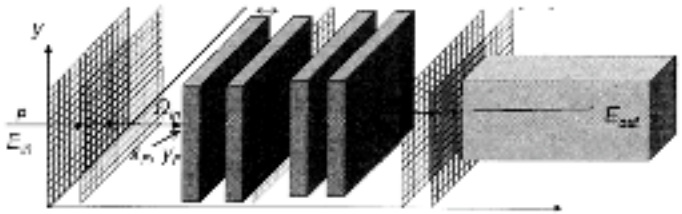


Fig. 2. Experimental layout: the 200 MeV proton beam enters from left, is analyzed in the entrance telescope, passes through the segmented absorber (12 pieces of PMMA of 1.25 cm thickness each), and is again analyzed in the exit telescope before being stopped in the crystal. For beam diagnostic tests, the PMMA is removed and for MLP determination, one of the entrance telescope planes is employed as a roving module.